In the Claims

Please cancel claims 1-132, and 138-140, without prejudice, to reduce the filing fee. Please replace all prior versions of the claims pursuant to 37 C.F.R. §1.121 as modified by 68 Fed. Reg. 38611 (June 30, 2003) as indicated below.

1-132. (canceled)

133. (Original) A method for identifying a molecule that binds a known target in a cell from a pool of candidate molecules, comprising:

(a) covalently bonding each molecule in the pool of candidate molecules to a methotrexate moiety or an analog of methotrexate to form a screening molecule;

(b) introducing the screening molecule into a cell which expresses a first fusion protein comprising a binding domain capable of binding methotrexate, a second fusion protein comprising the known target, and a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

(c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene;

(d) selecting which cell expresses the reporter gene; and

(e) identifying the small molecule that binds the known target.

134. (Original) The method of claim 133, wherein the cell is selected from the group consisting of insect cells, yeast cells, mammalian cell, and their lysates.

135. (Original) The method of claim 133, wherein the first or the second fusion protein comprises a transcription module selected from the group consisting of a DNA binding protein and a

transcriptional activator.

136. (Original) The method of claim 133, wherein the molecule is obtained from a combinatorial library.

137. (Original) The method of claim 133, wherein the steps (b)-(e) of the method are iteratively repeated in the presence of a preparation of random small molecules for competitive binding with the hybrid ligand so as to identify a molecule capable of competitively binding the known target.

138-140. (cancelled)

141. (Original) The method of claim 133, wherein the first fusion protein or the second fusion protein is DHFR-(DNA-binding domain).

142. (Original) The method of claim 133, wherein the first fusion protein or the second fusion protein is DHFR-LexA.

143. (Original) The method of claim 133, wherein the first fusion protein or the second fusion protein is DHFR-(transcription activation domain).

144. (Original) The method of claim 133, wherein the first fusion protein or the second fusion protein is DHFR-B42.

145. (Original) The method of claim 133, where the cell is a yeast cell, a bacteria cell or a mammalian cell.

146. (Original) The method of claim 133, where the cell is *S. cerevisiae* or *E. coli*.

147. (Original) A method for identifying a molecule that binds

a known target in a cell from a pool of candidate molecules, comprising:

(a) covalently bonding each molecule in the pool of candidate molecules to a methotrexate moiety to form a screening molecule;

(b) introducing the screening molecule into a cell which expresses a first fusion protein comprising a binding domain capable of binding methotrexate, a second fusion protein comprising the known target, and a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

(c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene;

(d) selecting which cell expresses the reporter gene; and

(e) identifying the small molecule that binds the known target.

148. (Original) The method of claim 147, wherein the cell is selected from the group consisting of insect cells, yeast cells, mammalian cell, and their lysates.

149. (Original) The method of claim 147, wherein the first or the second fusion protein comprises a transcription module selected from the group consisting of a DNA binding protein and a transcriptional activator.

150. (Original) The method of claim 147, wherein the molecule is obtained from a combinatorial library.

151. (Original) The method of claim 147, wherein the steps (b)-(e) of the method are iteratively repeated in the presence of a preparation of random small molecules for competitive binding with the hybrid ligand so as to identify a molecule capable of

competitively binding the known target.

152. (Original) The method of claim 147, wherein the first fusion protein or the second fusion protein is DHFR-(DNA-binding domain).

153. (Original) The method of claim 147, wherein the first fusion protein or the second fusion protein is DHFR-LexA.

154. (Original) The method of claim 147, wherein the first fusion protein or the second fusion protein is DHFR-(transcription activation domain).

155. (Original) The method of claim 147, wherein the first fusion protein or the second fusion protein is DHFR-B42.

156. (Original) The method of claim 147, where the cell is a yeast cell, a bacteria cell or a mammalian cell.

157. (Original) The method of claim 147, where the cell is *S. cerevisiae* or *E. coli*.